UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/034,650	12/20/2001	David W. Morris	529452000128	9852

7590 12/12/2005

GWILYM ATTWELL
COZEN O'CONNOR
1900 MARKET STREET
PHILADELPHIA, PA 19103

EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 12/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/034,650	MORRIS ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,18 and 20-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,18 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The Election filed 10/27/05 in response to the Office Action of 6/1/05 is acknowledged and has been entered. Applicant elected group VI and SEQ ID NO:59 with traverse.

The traversal is on the ground(s) that further grouping would not impose a serious burden on the examiner. For example, Applicants assert that two or more of the groups III-V or VII should be searched together, citing that the Office has chosen to limit the search to a single sequence. Applicants further note that groups II, IV, and VII were all classified in class 435, subclass 4. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the Office Action. Groups III and IV are drawn to distinct methods of screening, group V is drawn to a method of evaluating the effect of a drug, and group VII is drawn to a method of inhibition. Each of these inventions is unrelated as they comprise distinct steps and utilize different products, which demonstrates that each method has a different mode of operation. Searching and examining each of these methods would result in a serious burden on the examiner. Further, there are currently approximately eight different databases that accompany the results of a search of one discrete polynucleotide sequence and each result set from a particular database must be carefully considered. Hence, the search of multiple polynucleotides in the databases would require extensive searching and review and would invoke a high burden of search. Furthermore, it is

noted that the literature search, particularly relevant in this art, is not coextensive and is very important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 11, 18, and 20-25 are pending.

Claims 11, 18, and 20-25 are currently under consideration.

Claim Objections

Claim 11 is objected to for reciting "....the level of an expression product comprising an nucleotide sequence..." . It is suggested that "an", before "nucleotide sequence", is changed to "a". The word "an" in place of "a" should only be used before a word that begins with a vowel sound. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 18, and 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites "...a second unaffected individual...". It is unclear what Applicant means by "unaffected".

Claim 18 is incomplete. It is missing essential contact and correlation steps. It is unclear what the sample be contacted with in order to determine the sequence. It is also unclear what the sequence will be compared to or correlated with.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 18, and 20-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the

invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims are broadly drawn to a method of diagnosing every and any type of cancer and methods of determining whether a patient has a propensity to cancer by comparing the expression of a nucleotide having at least 95% sequence identity to SEQ ID NO:59 in one sample with another sample from a normal tissue type. The specification discloses that SEQ ID NO:59 is a cancer associated (CA) nucleic acid (page 2 lines 9-12 and Table 10, in particular) which encodes LFNG. The specification further discloses that CA nucleic acids were identified as insertion sites, in mice, for the murine leukemia virus (page 7 lines 20-23, in particular).

However, the specification lacks <u>any</u> working example *addressing* whether a polynucleotide having at least 95% sequence identity to SEQ ID NO:59 is aberrantly expressed in any cancer type. Further, the specification lacks any working example addressing whether measuring the expression of a nucleotide having at least 95% sequence identity to SEQ ID NO:59 can be used to determine whether a patient has a "propensity" to any type of cancer. Thus, claim 18 broadly encompasses assessing an individual's risk for developing cancer and the specification does not provide the

necessary guidelines or evidence that would predictably enable risk assessment. Thus, Applicant is not enabled for a method of diagnosing any type of carcinoma or determining whether a patient has a propensity to any cancer by comparing the expression of a nucleotide having at least 95% sequence identity to SEQ ID NO:59 in one sample with another sample from a normal tissue type.

Those of skill in the art also recognize that the diagnosis of cancer using specific biomarkers has many variables prior to any type of predictive success. Tockman et al (Cancer Research, 1992, 52:2711s-2718s) teaches considerations necessary to bring a cancer biomarker to successful clinical applications. Prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective populations trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and ***if validated*** can be used for population screening (page 2713s column 1, in particular). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid

intermediate end point marker (page 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (page 2716s column 2, in particular). In addition, Slamon et al. (Science, 1987, 235:177-182) teach other essential factors that are known to be important in the prognosis of cancer in individual patients such as size of primary tumor, stage of disease at diagnosis, hormonal receptor status, and number of axillary lymph nodes involved with disease (page 178 1st column second paragraph, in particular). Such data are critical for assessing actuarial curves for relapse (figure 3), and for comparing disease-free survival and overall survival to prognostic factors (table 4). For the reasons described above, Applicant has not demonstrated the ability to use SEQ ID NO:59 as a biomarker for any other type of cancer.

In view of the teachings above, and the lack of guidance or exemplification in the specification, it would not be predictable that the method could be performed as contemplated. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Claims 11, 18, and 20-25 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:59 and therefore the written description is not commensurate in scope with the claims which read on variants of SEQ ID NO:59.

The claims are drawn to polynucleotides having at least 95% sequence identity with SEQ ID NO:59. The specification also discloses that this sequence is a fragment of larger genes (see page 11 lines 38-39, in particular), which are not disclosed in the specification. The claims do not require that the polynucleotides possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. Further, there is no identification of any particular portion of the structure that must be conserved. Accordingly, in the

absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only methods comprising determining the expression level of polynucleotides comprising the nucleotide sequence set forth in SEQ ID NO: 59 and methods of sequencing polynucleotides comprising the nucleotide sequence set forth in SEQ ID NO: 59, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER